

AMENDMENTS TO THE CLAIMS:

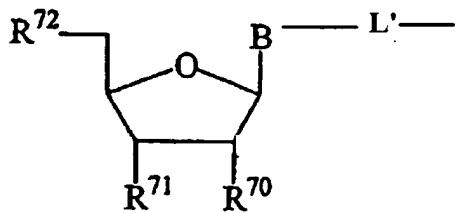
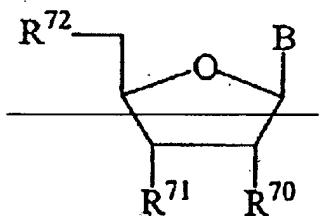
This listing of claims will replace all prior versions, and listings, of claims in the application.

LISTING OF CLAIMS:

Claims 1- 69 (canceled)

Claim 70 (currently amended): A labeled nucleoside/tide or nucleoside/tide analog ~~comprising a~~ ~~comprising a~~ rhodamine dye conjugated by a linker (L') to a nucleoside/tide or nucleoside/tide analog (NUC), wherein:

the rhodamine is a rhodamine-type parent xanthene having attached to the xanthene C9 carbon a phenyl group that is further substituted with an ortho carboxy or ortho sulfonate group or a salt thereof, one to three substituted or unsubstituted aminopyridinium groups and a substituted or unsubstituted alkylthio, or arylthio group; and the nucleoside/tide or nucleoside/tide analog and linker taken together comprise[[s]] the structure:



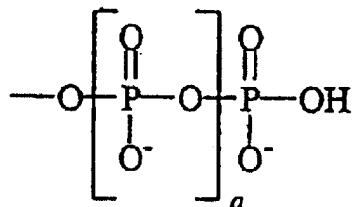
wherein:

B is a nucleobase selected from a purine, a 7-deazapurine, an 8-aza,7-deazapurine, a pyrimidine, a normal nucleobase and a common analog of a normal nucleobase;

L' is the linker;

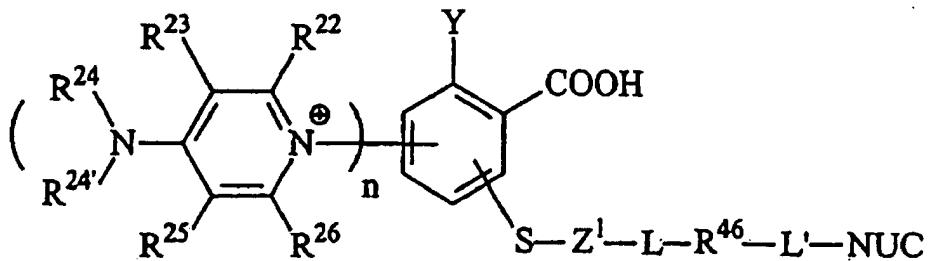
R⁷⁰ and R⁷¹, when taken alone, are each independently selected from hydrogen, hydroxyl and a moiety which blocks polymerase-mediated template-directed polymerization, or when taken together form a bond such that the illustrated sugar is 2',3'-didehydroribose; and

R⁷² is selected from hydroxyl, a phosphate ester having the formula:



where *a* is an integer from 0 to 2, and a phosphate ester analog, or a salt thereof.

Claim 71 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog of claim 70 comprising the formula:



wherein:

Y is a rhodamine-type parent xanthene ring attached to the illustrated phenyl group at the xanthene C9 carbon;

R²², R²³, R²⁵, and R²⁶ are independently selected from hydrogen and (C₁-C₆) alkyl;

R²⁴, when taken alone, is (C₁-C₆) alkyl, or when taken together with R^{24'} is (C₄-C₁₀) alkyldiyl, (C₄-C₆) alkylene, (C₄-C₆) heteroalkyldiyl and (C₄-C₆) heteroalkylene;

R^{24'}, when taken alone, is (C₁-C₆) alkyl, or when taken together with R²⁴ is (C₄-C₁₀) alkyldiyl, (C₄-C₆) alkylene, (C₄-C₆) heteroalkyldiyl and (C₄-C₆) heteroalkylene;

n is 1, 2, or 3;

S is sulfur;

Z¹ is selected from (C₁-C₁₂) alkyldiyl, (C₁-C₁₂) alkyldiyl independently substituted with one or more of the same or different W¹ groups, (C₅-C₁₄) aryldiyl, and (C₅-C₁₄) aryldiyl independently substituted with one or more of the same or different W² groups;

W¹ is selected from -X, -R, =O, -OR, -SR, =S, -NRR, =NR, -CX₃, -CN, -OCN, -SCN, -NCO, -NCS, -NO, -NO₂, =N₂, -N₃, -S(O)₂O⁻, -S(O)₂OH, -S(O)₂R, -C(O)R, -C(O)X, -C(S)R, -C(S)X, -C(O)OR, -C(O)O⁻, -C(S)OR, -C(O)SR, -C(S)SR, -C(O)NRR, -C(S)NRR AND -C(NR)NRR;

W² is selected from -R, -OR, -SR, -NRR, -S(O)₂O⁻, -S(O)₂OH, -S(O)₂R, -C(O)R, -C(O)X, -C(S)R, -C(S)X, -C(O)OR, -C(O)O⁻, -C(S)OR, -C(O)SR, -C(S)SR, -C(O)NRR, -C(S)NRR and -C(NR)NRR;

L is selected from a bond, (C₁-C₁₂) alkyldiyl, (C₁-C₁₂) substituted alkyldiyl, (C₆-C₂₆) arylalkyldiyl, -O-, -S-, -NR-, -C(O)O-, -C(O)NR-, -NRS(O)₂-, -NR-NR-, -NRC(O)O-, and -NRC(O)NR-;

R⁴⁶ is selected from -C(O)NR-, -C(O)O-, and -C(O)S-,

L' is selected from (C₁-C₂₀) alkyldiyl, (C₁-C₂₀) heteroalkyldiyl, (C₁-C₂₀) alkylene, (C₁-C₂₀) heteroalkylene, (C₆-C₂₆) arylalkyldiyl, (C₅-C₂₀) heteroarylalkyldiyl, and substituted forms thereof; and

NUC is a nucleoside/tide or nucleoside/tide analog;

Applicants: Lee *et al.*

Appl. Serial No.: 10/007,253

Filing Date: October 24, 2001

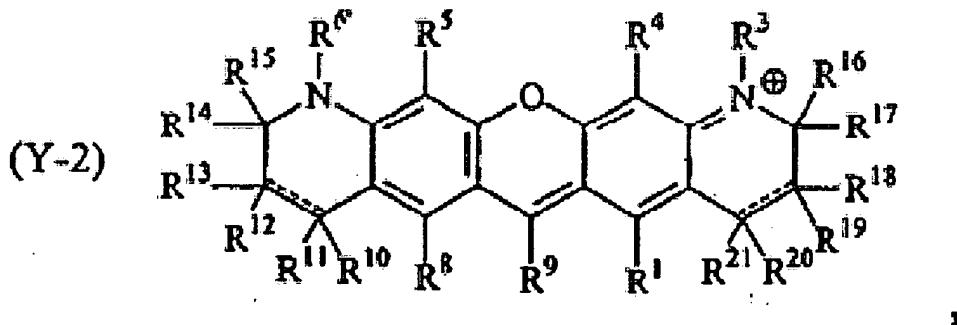
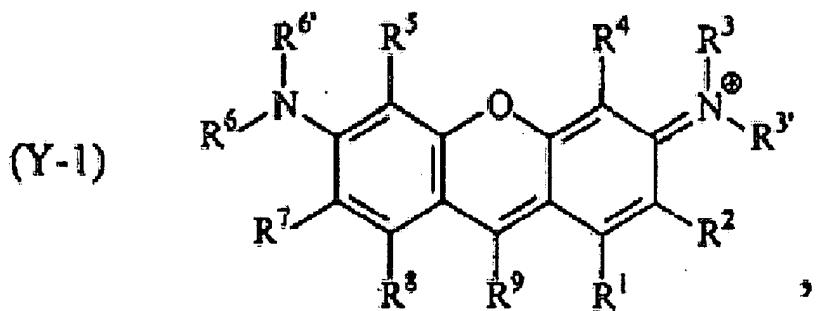
Amendment and Reply to Office Action

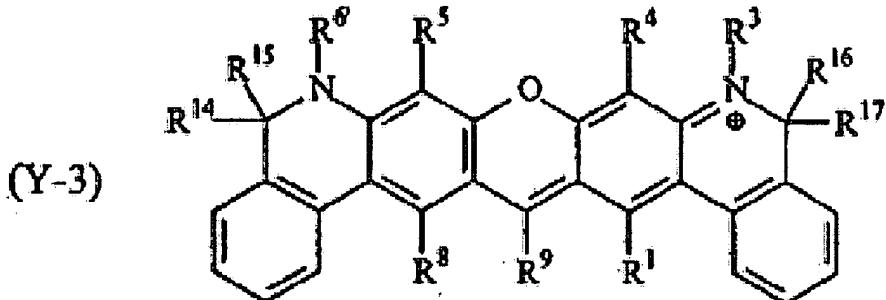
January 13, 2004

Page 7 of 34

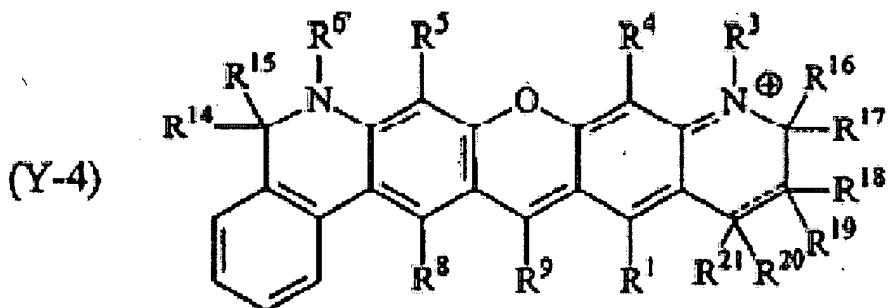
each R is independently selected from hydrogen, (C₁-C₆) alkyl, (C₅-C₂₀) aryl, (C₆-C₂₆) arylalkyl, and (C₅-C₂₀) arylaryl; or when two R groups on the same nitrogen atom are taken together, those two R groups are (C₄-C₁₀) alkyldiyl or (C₄-C₁₀) alkylene; and each X is independently a halogen.

Claim 72 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog of claim 71 wherein Y comprises the rhodamine-type parent xanthene ring structures:





, and



and a salt thereof, wherein:

R¹ and R² when taken alone, are independently hydrogen or (C₁-C₆) alkyl;

R³ and R^{3'} when taken alone, are independently selected from hydrogen, (C₁-C₆) alkyl, (C₅-C₁₄) aryl and (C₅-C₁₄) arylaryl, or when taken together is (C₄-C₆) alkyldiyl or (C₄-C₆) alkylene, or when individually taken together with R² or R⁴ is (C₂-C₆) alkyldiyl or (C₂-C₆) alkylene;

R⁴, when taken alone, is selected from hydrogen and (C₁-C₆) alkyl, or when taken together with R³ or R^{3'} is (C₂-C₆) alkyldiyl or (C₂-C₆) alkylene;

R⁵, when taken alone, is selected from hydrogen and (C₁-C₆) alkyl, or when taken together with R⁶ or R^{6'} is (C₂-C₆) alkyldiyl or (C₂-C₆) alkylene;

R⁶ and R^{6'} when taken alone, are selected from hydrogen, (C₁-C₆) alkyl, (C₅-C₁₄) aryl and arylaryl, or when taken together are (C₄-C₆) alkyldiyl or alkylene, or when individually taken together with R⁵ or R⁷ is (C₂-C₆) alkyldiyl or alkylene;

Applicants: Lee *et al.*

Appl. Serial No.: 10/007,253

Filing Date: October 24, 2001

Amendment and Reply to Office Action

January 13, 2004

Page 9 of 34

R^7 , when taken alone, is selected from hydrogen and (C_1 - C_6) alkyl, or when taken together with R^6 or $R^{6'}$ is (C_2 - C_6) alkyldiyl or alkylene;

R^8 , when taken alone, is selected from hydrogen and (C_1 - C_6) alkyl;

R^{10} , R^{11} , R^{12} , R^{13} , R^{14} , R^{15} , R^{16} , R^{17} , R^{18} , R^{19} , R^{20} and R^{21} are each independently selected from hydrogen and (C_1 - C_6) alkyl, or

when R^{10} , R^{11} , R^{12} and R^{13} taken together are (C_5 - C_{14}) aryleno or (C_5 - C_{14}) aryleno substituted with one or more of the same or different (C_1 - C_6) alkyl, or

when R^{18} , R^{19} , R^{20} and R^{21} taken together are (C_5 - C_{14}) aryleno or aryleno substituted with one or more of the same or different (C_1 - C_6) alkyl; and

R^9 is the point of attachment to the xanthene C9 carbon.

Claim 73 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog of claim 72 wherein R^2 when taken together with R^3 or $R^{3'}$ is (C_2 - C_6) alkyldiyl or (C_2 - C_6) alkylene.

Claim 74 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog of claim 72 wherein:

an alkyldiyl or alkylene bridge formed by taking R^2 together with R^3 or $R^{3'}$, R^7 together with R^6 or $R^{6'}$, or R^4 together with R^3 or $R^{3'}$, is ethano, propano, 1,1-dimethylethano, 1,1-dimethylpropano or 1,1,3-trimethylpropano;

an aryleno bridge formed by taking R^1 together with R^2 is benzo or naphtho;

an alkyldiyl or alkylene bridge formed by taking R^3 together with $R^{3'}$, or R^6 together with $R^{6'}$, is butano;

an alkyldiyl or alkylene bridge formed by taking R^5 together with R^6 or $R^{6'}$; is ethano, propano, 1,1-dimethylethano, 1,1-dimethylpropano and 1,1,3-trimethylpropano; and

an aryleno bridge formed by taking R^{10} , R^{11} , R^{12} and R^{13} together, or R^{18} , R^{19} , R^{20} and R^{21} together, is benzo.

Applicants: Lee *et al.*

Appl. Serial No.: 10/007,253

Filing Date: October 24, 2001

Amendment and Reply to Office Action

January 13, 2004

Page 10 of 34

Claim 75 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog of claim 71 in which Z¹ is phenyldiyl.

Claim 76 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog of Claim 71 in which L' is selected from: $-\text{C}\equiv\text{C}-\text{CH}_2-$ and $-\text{C}\equiv\text{C}-\text{CH}_2-\text{O}-\text{CH}_2\text{CH}_2-$

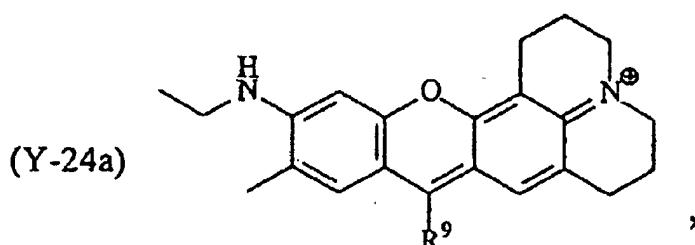
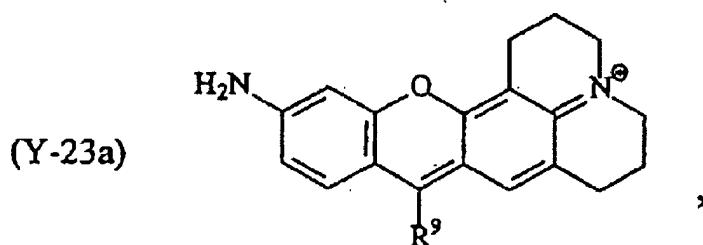
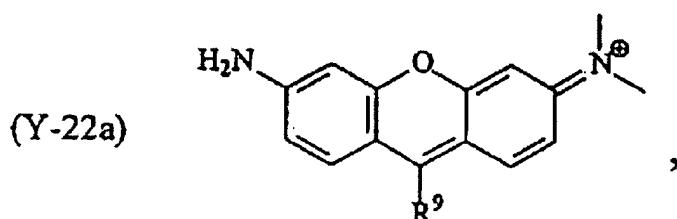
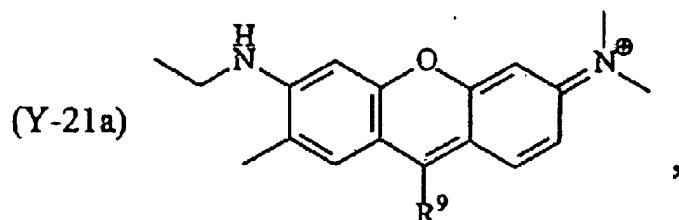
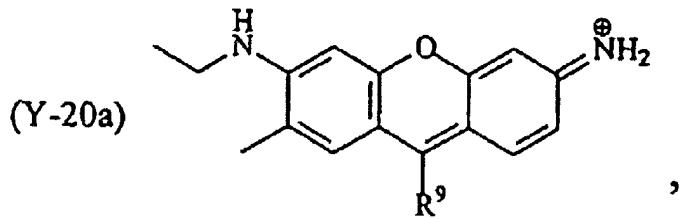
Claim 77 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog

of Claim 71 in which L' is: $-\text{C}\equiv\text{C}-\text{CH}_2-\text{O}-\text{CH}_2\text{CH}_2-\overset{\text{R}^{47}}{\underset{\text{N}}{\text{N}}}-\text{R}^{48}-$ wherein R⁴⁷ is hydrogen or (C₁-C₆) alkyl, and R⁴⁸ is selected from:



wherein each r is independently an integer from 1 to 6; R⁴⁹ is hydrogen, (C₁-C₆) alkyl, or an amino acid side chain; and φ is phenyldiyl or substituted phenyldiyl.

Claim 78 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog of claim 71 in which Y is selected from the structures:



Applicants: Lee *et al.*

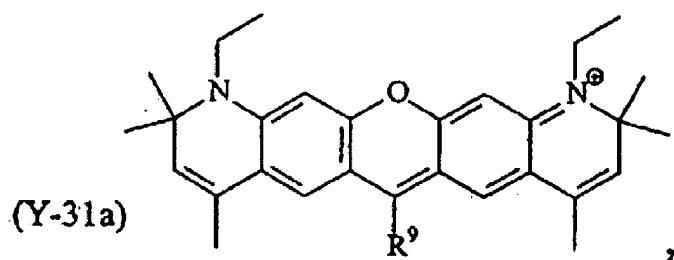
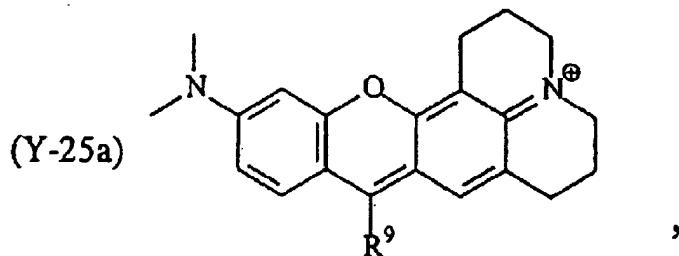
Appl. Serial No.: 10/007,253

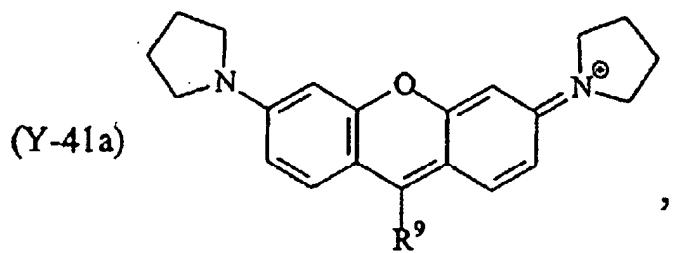
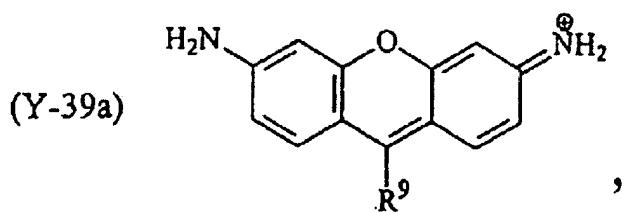
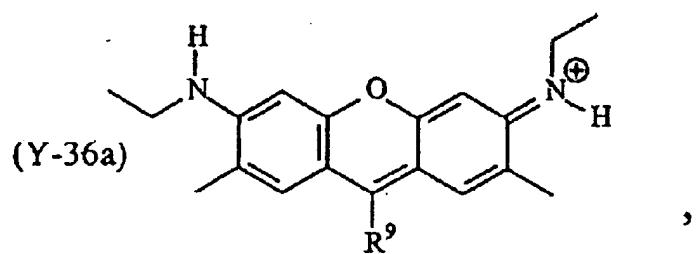
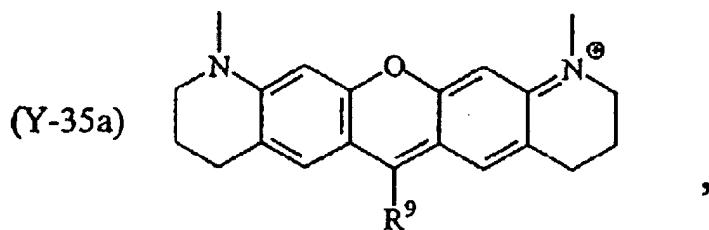
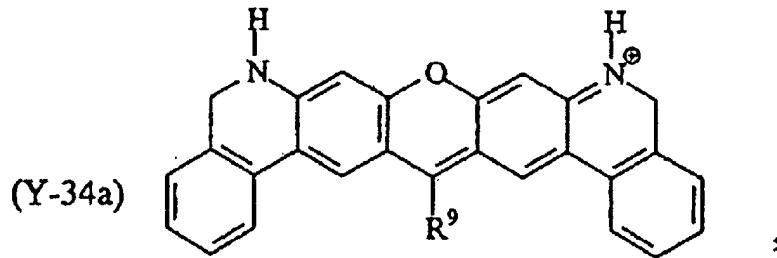
Filing Date: October 24, 2001

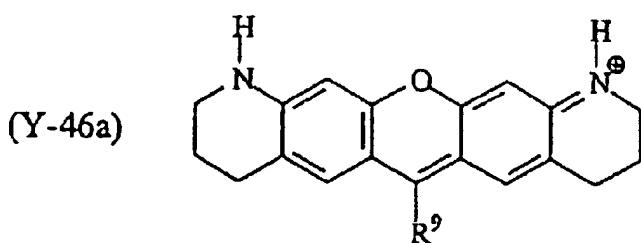
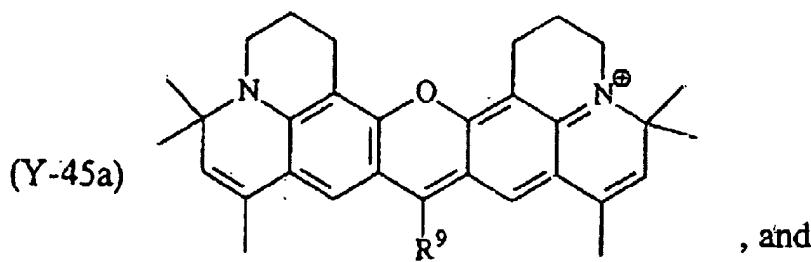
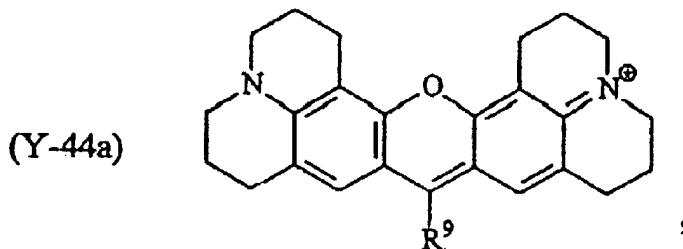
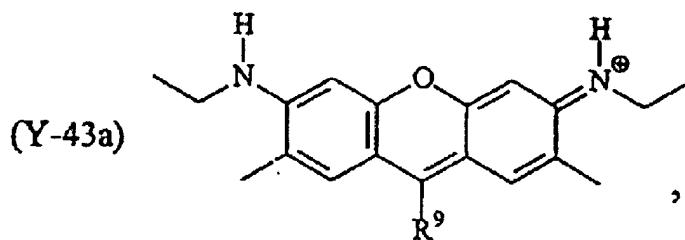
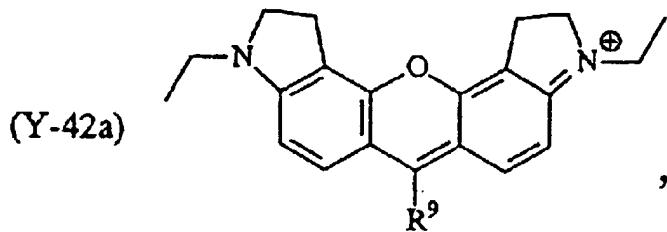
Amendment and Reply to Office Action

January 13, 2004

Page 12 of 34

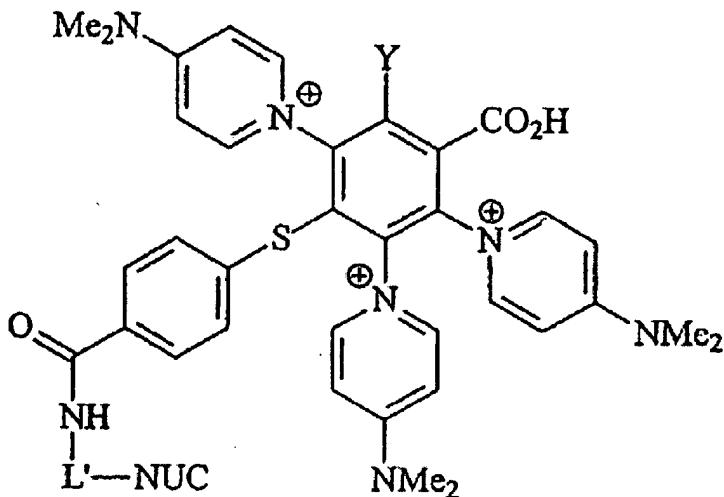






Claim 79 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog of claim 71 wherein R²², R²³, R²⁵, and R²⁶ are each hydrogen.

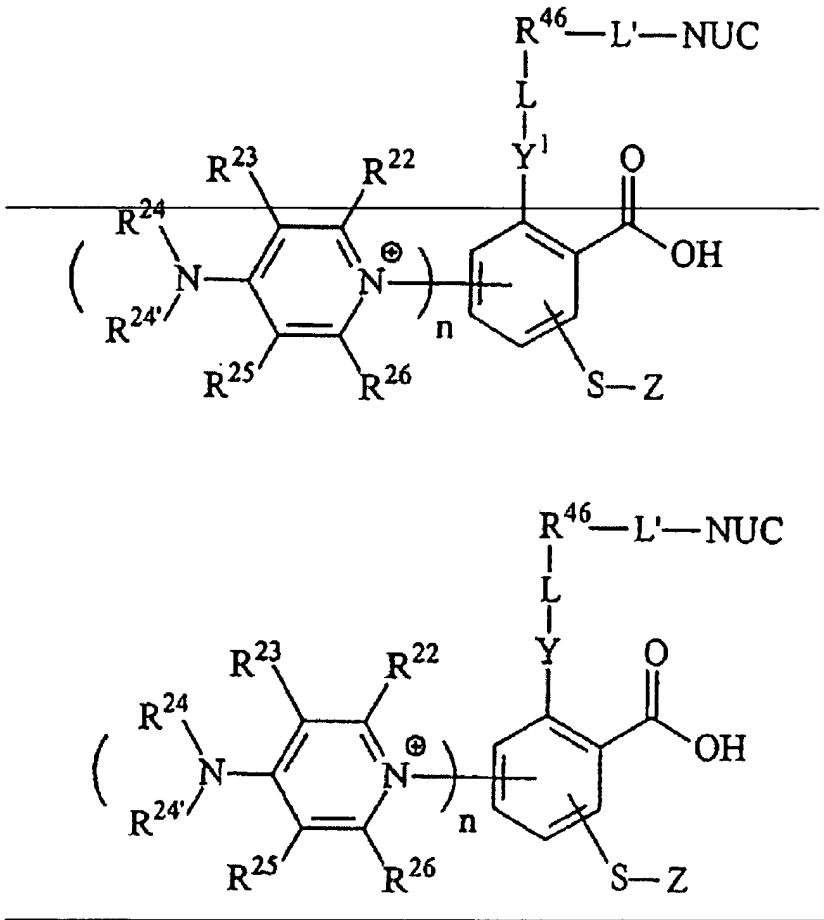
Claim 80 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog of claim 71 which comprises the structure:



or a salt thereof.

Claim 81 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog of Claim 80 in which L' is selected from: $-\text{C}\equiv\text{C}-\text{CH}_2-$ and $-\text{C}\equiv\text{C}-\text{CH}_2-\text{O}-\text{CH}_2\text{CH}_2-$.

Claim 82 (currently amended): The labeled nucleoside/tide or nucleoside/tide analog of claim 70 comprising the formula:



wherein:

[[Y¹]] Y is a rhodamine-type parent xanthene ring attached to the illustrated phenyl group at the xanthene C9 carbon;

R²², R²³, R²⁵, and R²⁶ are independently selected from hydrogen and (C₁-C₆) alkyl;

R²⁴, when taken alone, is (C₁-C₆) alkyl, or when taken together with R^{24'} is (C₄-C₁₀) alkylidyl, (C₄-C₆) alkylene, (C₄-C₆) heteroalkylidyl or (C₄-C₆) heteroalkylene;

R^{24'}, when taken alone, is (C₁-C₆) alkyl, or when taken together with R²⁴ is (C₄-C₁₀) alkylidyl, (C₄-C₆) alkylene, (C₄-C₆) heteroalkylidyl or (C₄-C₆) heteroalkylene;

Applicants: Lee *et al.*

Appl. Serial No.: 10/007,253

Filing Date: October 24, 2001

Amendment and Reply to Office Action

January 13, 2004

Page 17 of 34

n is 1, 2, or 3;

S is sulfur;

Z is (C₁-C₁₂) alkyl, (C₁-C₁₂) alkyl substituted with one or more of the same or different W¹ groups, (C₅-C₂₀) aryl, and (C₅-C₂₀) aryl substituted with one or more of the same or different W² groups;

W¹ is selected from -X, -R, =O, -OR, -SR, =S, -NRR, =NR, -CX₃, -CN, -OCN, -SCN, -NCO, -NCS, -NO, -NO₂, =N₂, -N₃, -S(O)₂O⁻, -S(O)₂OH, -S(O)₂R, -C(O)R, -C(O)X, -C(S)R, -C(S)X, -C(O)OR, -C(O)O⁻, -C(S)OR, -C(O)SR, -C(S)SR, -C(O)NRR, -C(S)NRR and -C(NR)NRR;

W² is selected from -R, -OR, -SR, -NRR, -S(O)₂O⁻, -S(O)₂OH, -S(O)₂R, -C(O)R, -C(O)X, -C(S)R, -C(S)X, -C(O)OR, -C(O)O⁻, -C(S)OR, -C(O)SR, -C(S)SR, -C(O)NRR, -C(S)NRR and -C(NR)NRR;

L is selected from a bond, (C₁-C₁₂) alkyldiyl, (C₁-C₁₂) substituted alkyldiyl, (C₆-C₂₆) arylalkyldiyl, -O-, -S-, -NR-, -C(O)O-, -C(O)NR-, -NRS(O)₂-, -NR-NR-, -NRC(O)O-, and -NRC(O)NR-;

R⁴⁶ is selected from -C(O)NR-, -C(O)O-, and -C(O)S,

L' is selected from (C₁-C₂₀) alkyldiyl, (C₁-C₂₀) heteroalkyldiyl, (C₁-C₂₀) alkylene, (C₁-C₂₀) heteroalkylene, (C₆-C₂₆) arylalkyldiyl, (C₅-C₂₀) heteroarylalkyldiyl, and substituted forms thereof; and

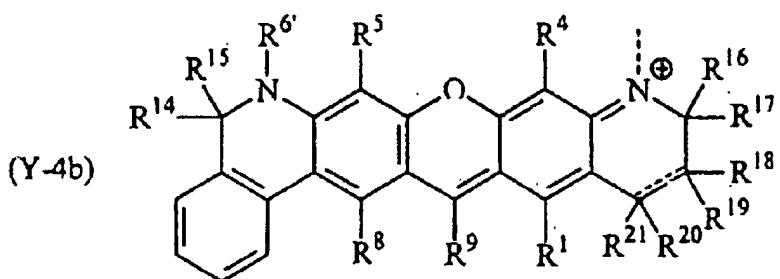
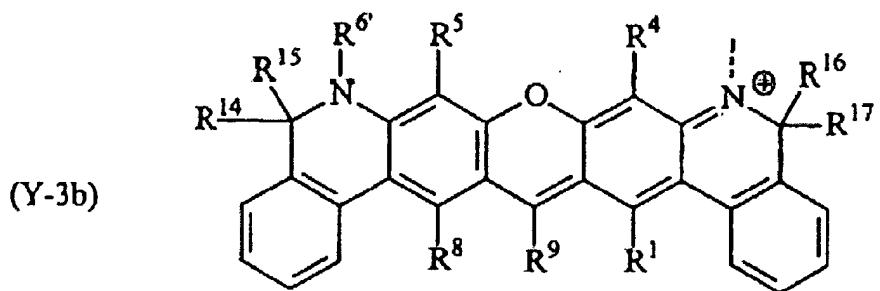
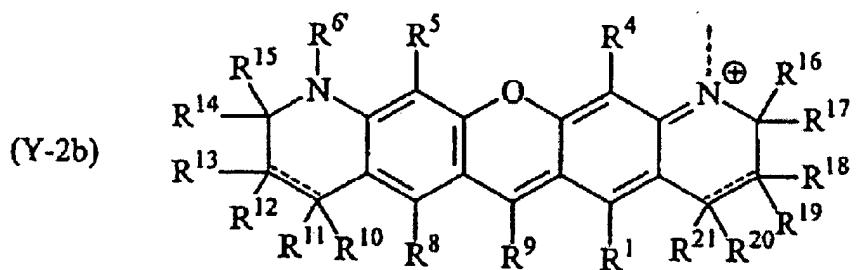
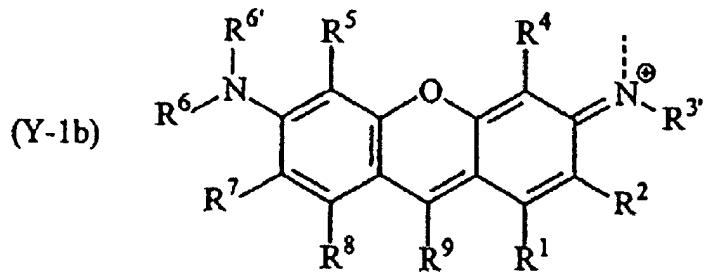
NUC is a nucleoside/tide or nucleoside/tide analog;

each R is independently selected from hydrogen, (C₁-C₆) alkyl, (C₅-C₂₀) aryl, (C₆-C₂₀) arylalkyl, and (C₆-C₂₀) arylaryl; or when two R groups on the same nitrogen atom are taken together, those two R groups are (C₄-C₁₀) alkyldiyl or (C₄-C₁₀) alkylene; and

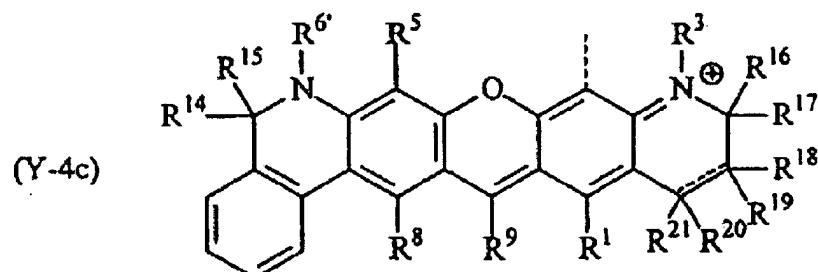
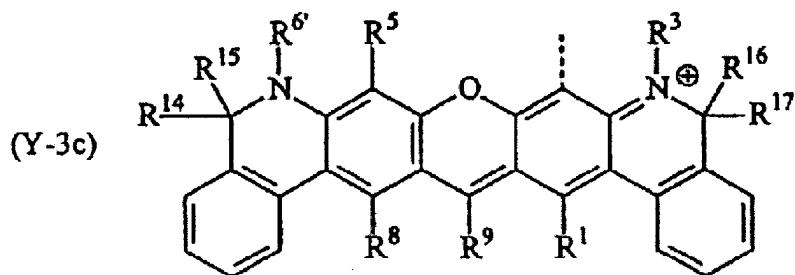
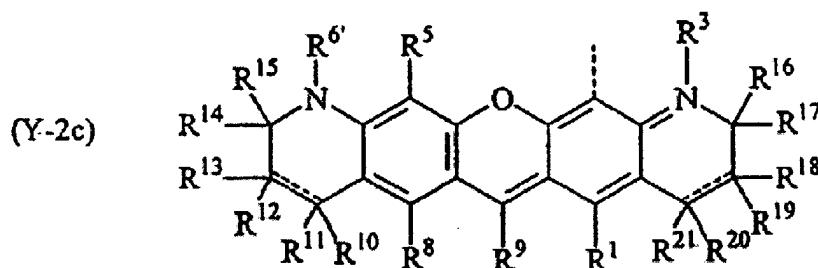
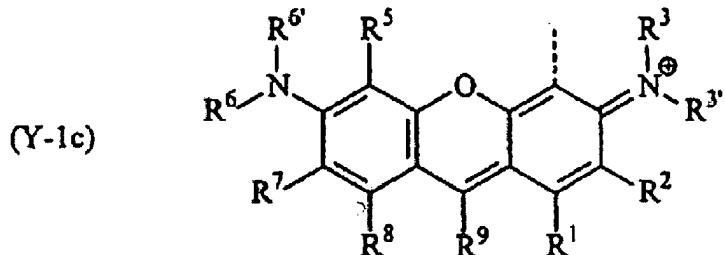
each X is independently a halogen.

Claim 83 (currently amended): The labeled nucleoside/tide or nucleoside/tide analog of Claim 82 in which [[Y¹]] Y is selected from:

Applicants: Lee *et al.*
Appl. Serial No.: 10/007,253
Filing Date: October 24, 2001
Amendment and Reply to Office Action
January 13, 2004
Page 18 of 34



Applicants: Lee *et al.*
Appl. Serial No.: 10/007,253
Filing Date: October 24, 2001
Amendment and Reply to Office Action
January 13, 2004
Page 19 of 34



wherein the dashed line at the nitrogen or C4 atom indicates the point of attachment of L.

Claim 84 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog of claim 82 wherein:

an alkyldiyl or alkylene bridge formed by taking R² together with R³, R⁴ together with R^{3'}, R⁵ together with R⁶, or R⁷ together with R^{6'}, is ethano, propano, 1,1-dimethylethano, 1,1-dimethylpropano or 1,1,3-trimethylpropano; and

an arylene bridge formed by taking R¹⁰, R¹¹, R¹² and R¹³ together or R¹⁸, R¹⁹, R²⁰ and R²¹ together is benzo.

Claim 85 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog of claim 82 in which L is selected from phenyldiyl and naphthyldiyl.

Claim 86 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog of claim 82 in which L is -(CH₂)_i-φ- where i is an integer from 1 to 6 and φ is phenyldiyl or naphthyldiyl.

Claim 87 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog of claim 82 in which Z is selected from phenyl, benzyl, naphthyl, pyridyl and purinyl.

Claim 88 (currently amended): The labeled nucleoside/tide or nucleoside/tide analog of
Claim 82 in which L' is selected from: —C≡C—CH₂— and
—C≡C—CH₂—O—CH₂CH₂—.

Claim 89 (currently amended): The labeled nucleoside/tide or nucleoside/tide analog of

Claim 82 in which L' is: —C≡C—CH₂—O—CH₂CH₂—N—R⁴⁸— wherein R⁴⁷ is hydrogen or (C₁—C₆) (C₁—C₅) alkyl, and R⁴⁸ is selected from:

Applicants: Lee *et al.*

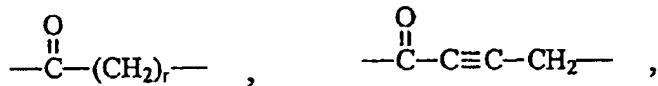
Appl. Serial No.: 10/007,253

Filing Date: October 24, 2001

Amendment and Reply to Office Action

January 13, 2004

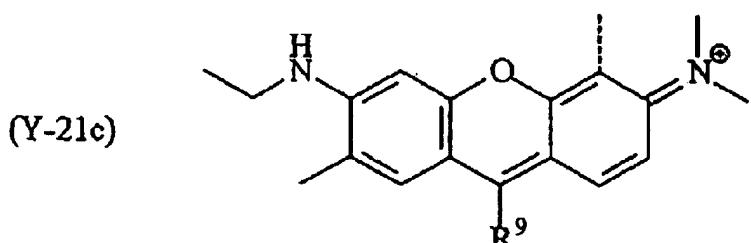
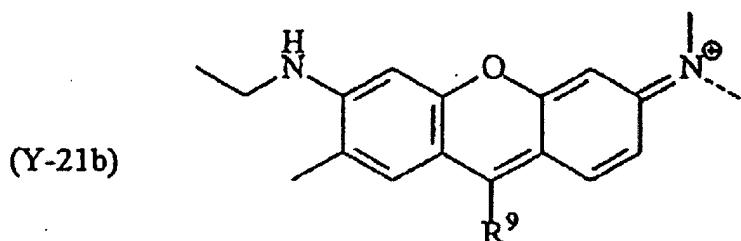
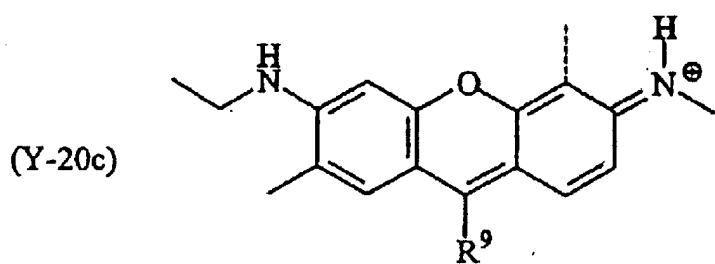
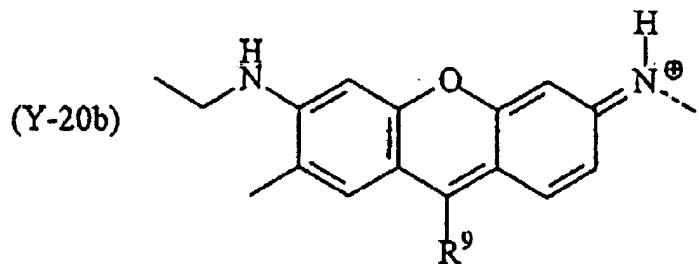
Page 21 of 34

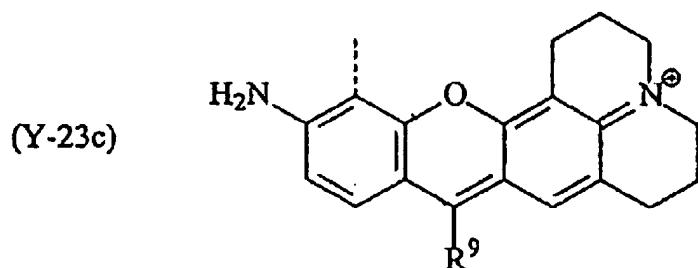
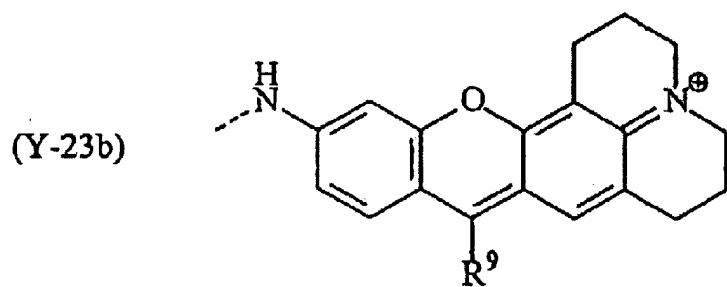
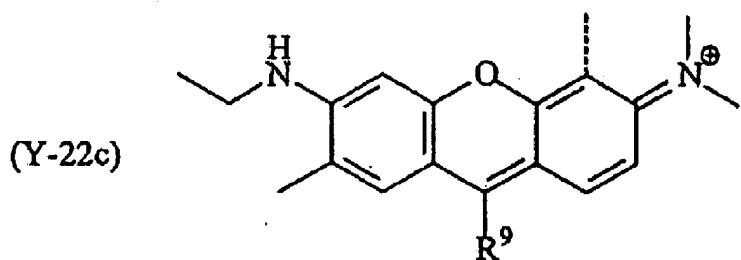
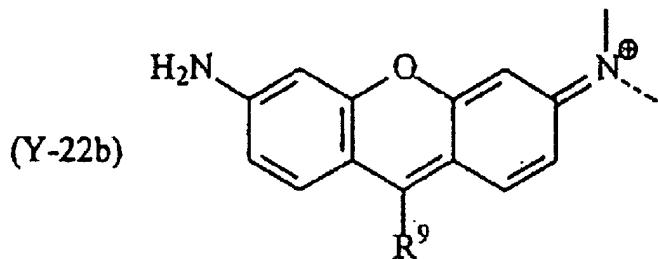


wherein each r is independently an integer from 1 to 6, R⁴⁹ is hydrogen, (C₁-C₆) alkyl, or an amino acid side chain; and φ is phenyldiyl or substituted phenyldiyl.

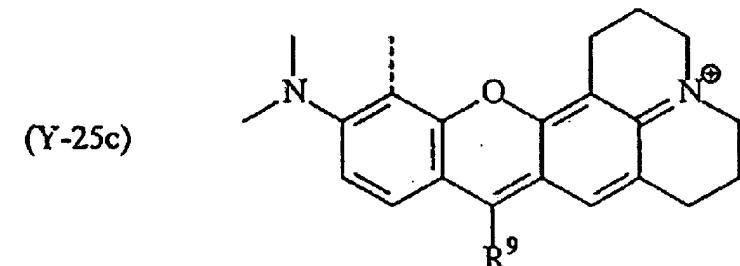
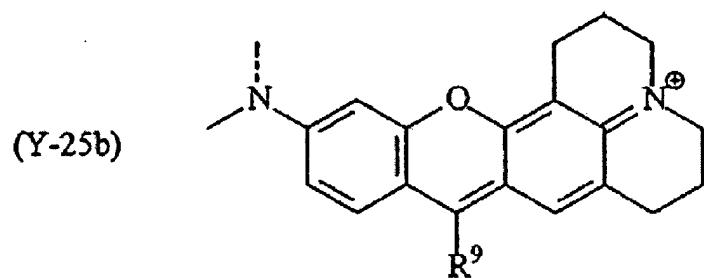
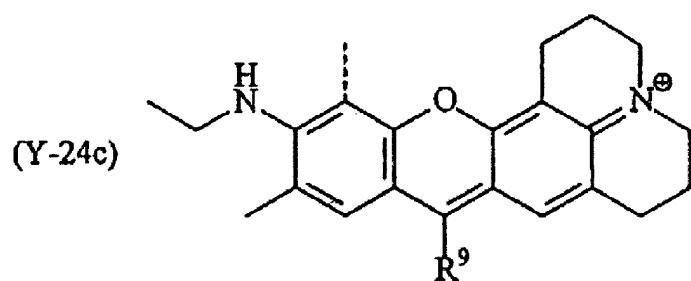
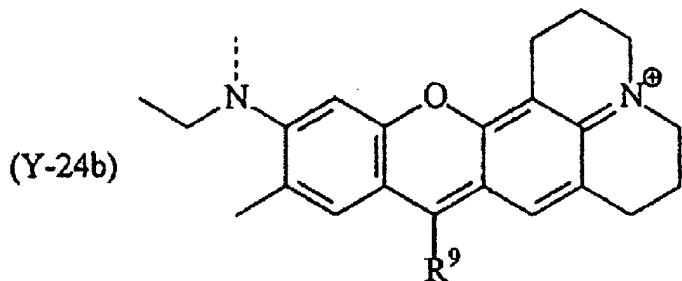
Claim 90 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog of claim 82 wherein R²², R²³, R²⁵, and R²⁶ are each hydrogen.

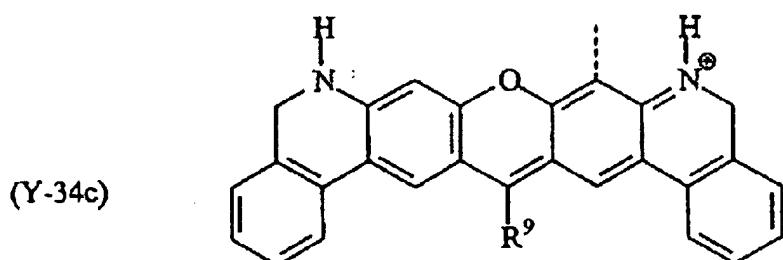
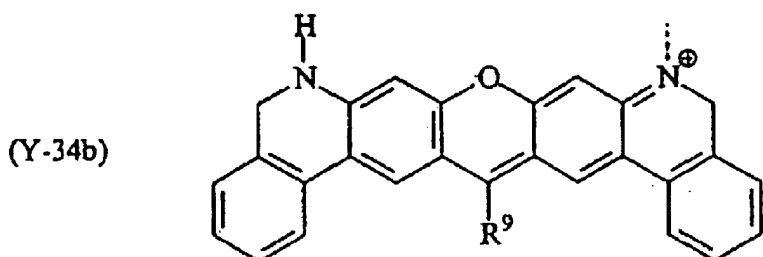
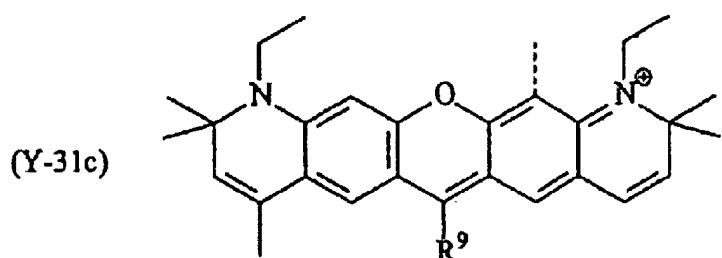
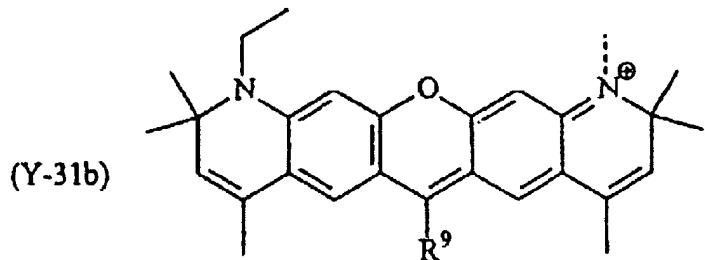
Claim 91 (currently amended): The labeled nucleoside/tide or nucleoside/tide analog of claim 82 in which [[Y¹]] Y is selected from the group consisting of:

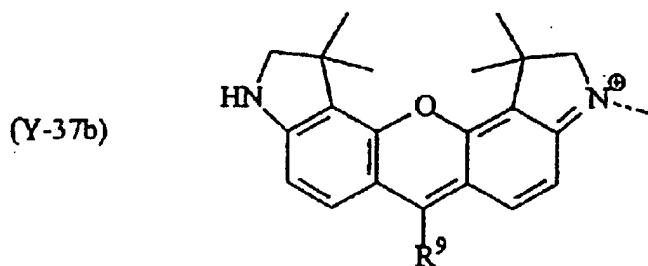
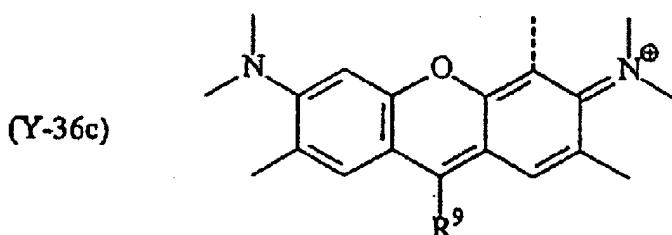
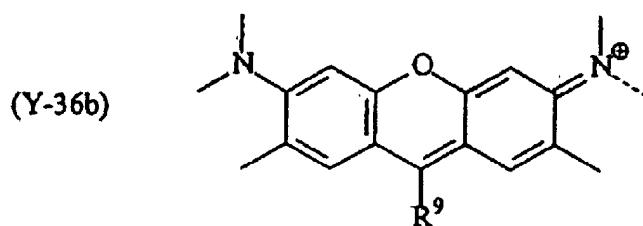
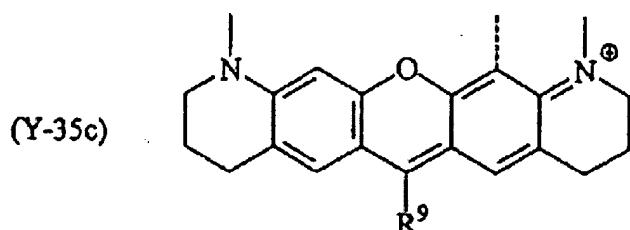
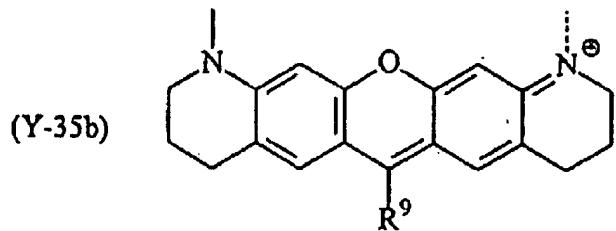


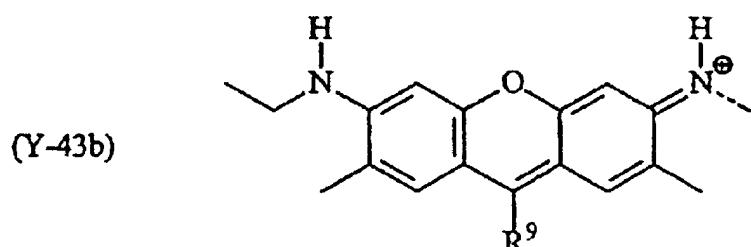
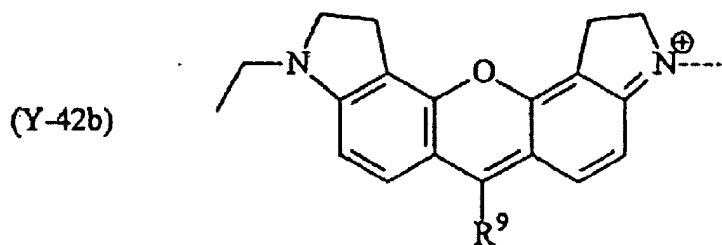
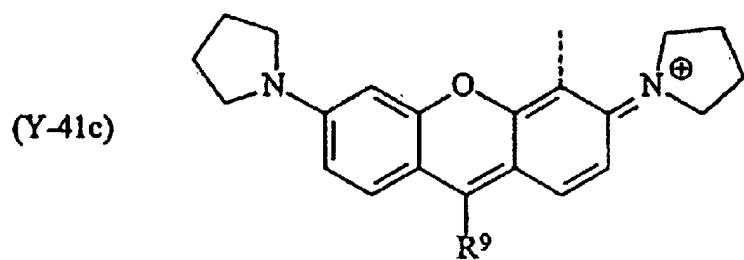
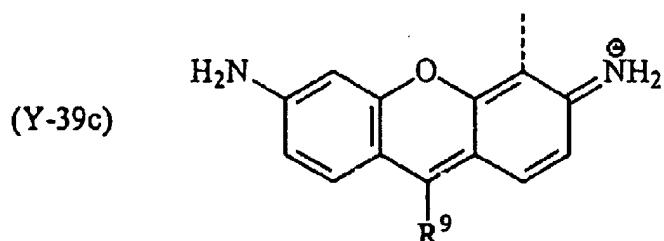
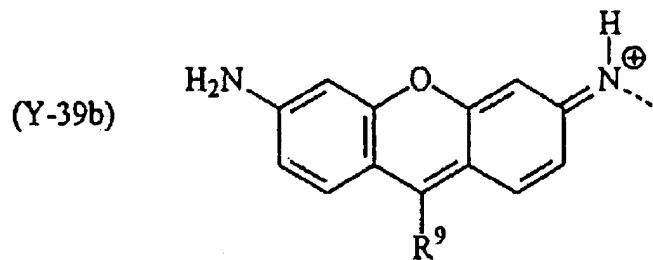


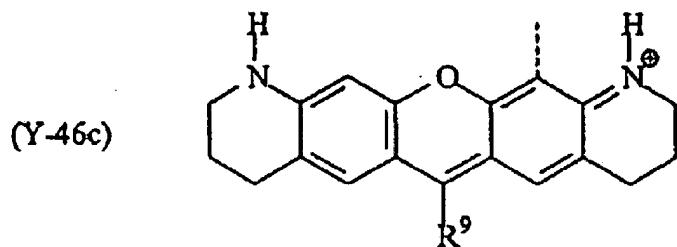
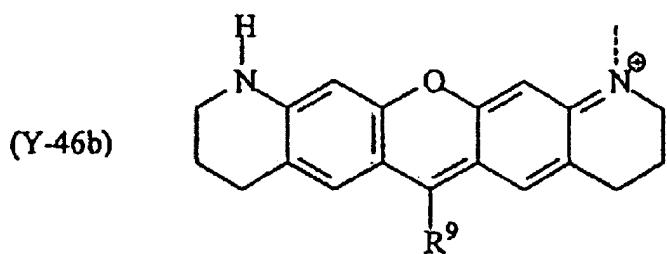
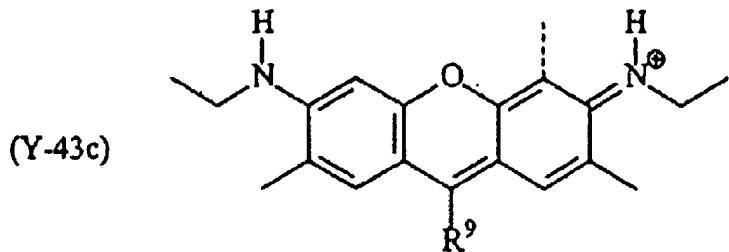
Applicants: Lee *et al.*
Appl. Serial No.: 10/007,253
Filing Date: October 24, 2001
Amendment and Reply to Office Action
January 13, 2004
Page 24 of 34





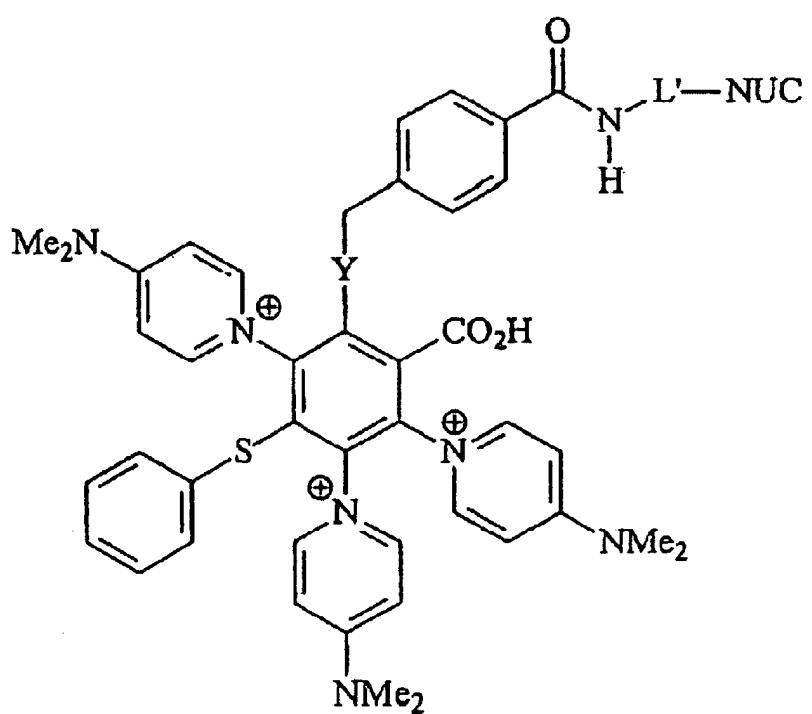
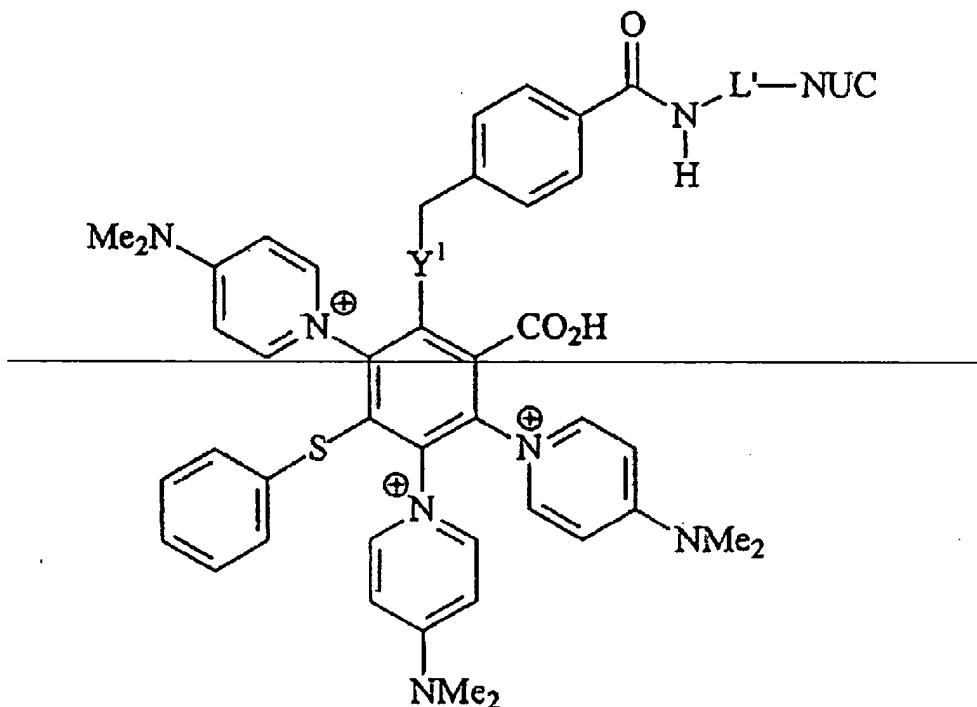






wherein the dash at the nitrogen or C4 atom indicates the point of attachment of L.

Claim 92 (currently amended): The labeled nucleoside/tide or nucleoside/tide analog of Claim 82 which has the structure:



Claim 93 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog of Claim 92 in which L' is selected from: $-\text{C}\equiv\text{C}-\text{CH}_2-$ and $-\text{C}\equiv\text{C}-\text{CH}_2-\text{O}-\text{CH}_2\text{CH}_2-$.

Claim 94 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog of Claim 70 further comprising a donor dye or an acceptor dye whereby the rhodamine dye and the donor dye or acceptor dye form an energy-transfer dye pair.

Claim 95 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog of Claim 94 wherein the donor dye or acceptor dye is a fluorescein, rhodamine, cyanine, phthalocyanine or squaraine.

Claim 96 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog of Claim 94 wherein the donor dye or acceptor dye is 4'-aminomethyl-6-carboxyfluorescein and the 4'-aminomethyl-6-carboxyfluorescein is covalently attached to the rhodamine dye by a linker.

Claim 97 (currently amended): The labeled nucleoside/tide or nucleoside/tide analog of Claim 96 wherein the aminomethylfluorescein is further covalently attached by a linker $[\text{L}]$ to the nucleobase B of the nucleoside/tide or nucleoside/tide analog.

Claim 98 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog of Claim 70 which is enzymatically incorporatable.

Claim 99 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog of Claim 70 which is a terminator.

Claim 100 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog

of Claim 70 which is enzymatically extendable.

Claim 101 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog of Claim 70 wherein R⁷¹ and R⁷⁰ are hydrogen.

Claim 102 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog of Claim 70 wherein R⁷¹ and R⁷⁰ are hydroxyl.

Claim 103 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog of Claim 70 wherein R⁷¹ is hydroxyl, and R⁷⁰ is hydrogen.

Claim 104 (previously presented): The labeled nucleoside/tide or nucleoside/tide analog of Claim 70 in which nucleobase B is selected from adenine, 7-deazaadenine, cytosine, guanine, 7-deazaguanine, thymine and uracil.

Claim 105 (previously presented): A labeled polynucleotide or polynucleotide analog comprising a rhodamine dye conjugated to a nucleoside/tide or nucleoside/tide analog, wherein the rhodamine is a rhodamine-type parent xanthene having attached to the xanthene C9 carbon a phenyl group that is further substituted with an ortho carboxy or ortho sulfonate group or a salt thereof, one to three substituted or unsubstituted aminopyridinium groups and a substituted or unsubstituted alkylthio, or arylthio group.